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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C12N 15/29, C07K 14/415, A61K 39/36, G01N 33/68</b>		A1	(11) International Publication Number: <b>WO 96/13589</b>
			(43) International Publication Date: 9 May 1996 (09.05.96)
(21) International Application Number: PCT/US95/14362			(81) Designated States: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG).
(22) International Filing Date: 24 October 1995 (24.10.95)			
(30) Priority Data: 08/330,275 27 October 1994 (27.10.94) US 08/460,039 2 June 1995 (02.06.95) US			
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(74) Agents: REMILLARD, Jane, E. et al.; Lahive & Cockfield, 60 State Street, Boston, MA 02109 (US).			<b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: T CELL EPITOPES OF THE MAJOR ALLERGENS FROM AMBROSIA ARTEMISIIFOLIA			
(57) Abstract <p>The present invention provides isolated peptides of the major protein allergens of <i>Ambrosia artemisiifolia</i>, or short ragweed pollen. Peptides within the scope of the invention comprise at least one T cell epitope, or preferably at least two T cell epitopes of a protein allergen selected from the allergens Amb a I.1, Amb a I.2, Amb a I.3, Amb a I.4 and Amb a II. Modified peptides having similar or enhanced therapeutic properties as the corresponding, naturally-occurring allergen or portion thereof, but having reduced side effects are disclosed. The invention also provides nucleic acids having sequences encoding peptides of the invention. Methods of treatment or of diagnosis of sensitivity to ragweed pollen allergens in an individual and therapeutic compositions comprising one or more peptides of the invention are also provided including multipetide formulations for human therapeutic use.</p>			

(v) FRAGMENT TYPE: internal

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

Asn Lys Asp Val Leu Glu Asn Gly Ala Ile Phe Val Ala Ser  
1 5 10

(2) INFORMATION FOR SEQ ID NO:66:

15 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 11 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

Val Leu Glu Asn Gly Ala Ile Phe Val Ala Ser  
1 5 10

30

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 11 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (v) FRAGMENT TYPE: internal

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

45      Leu Glu Asn Gly Ala Ile Phe Val Ala Ser Gly  
          1                         5                         10

(2) INFORMATION FOR SEQ ID NO:68:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 14 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: peptide

(v) FRAGMENT TYPE: internal

16. All or a portion of a modified peptide of claim 13 which does not bind immunoglobulin E specific for *Amb a* I.1 in a substantial percentage of individuals sensitive to *Amb a* I.1, or if binding of the peptide to said immunoglobulin E occurs, such binding does not result in release of mediators from mast cells or basophils in a substantial percentage of individuals sensitive to *Amb a* I.1.

17. All or a portion of a modified peptide of claim 13 which binds immunoglobulin E to a substantially lesser extent than *Amb a* I.1 binds said immunoglobulin E.

18. All or a portion of a modified peptide of claim 13 which modifies, in a ragweed pollen-sensitive individual to whom it is administered, the allergic response of the individual to *Amb a* I.1.

19. All or a portion of an isolated peptide of *Ambrosia artemisiifolia*, said peptide or portion thereof comprising at least one T cell epitope of *Ambrosia artemisiifolia*, said peptide comprising an amino acid sequence selected from the group consisting of:

- a) RAE 67.1 (SEQ ID NO:13);
- b) RAE 57.1 (SEQ ID NO:14);
- c) RAE 24.E (SEQ ID NO:15);
- d) RAE 24.1 (SEQ ID NO:16);
- e) RAE 22.E (SEQ ID NO:17);
- f) RAE 22.E-1 (SEQ ID NO:18);
- g) RAE 3.1 (SEQ ID NO:20);
- h) RAE 22.E-2 (SEQ ID NO:21);
- i) RAE 5.D (SEQ ID NO:22);
- j) RAE 6.D (SEQ ID NO:23);
- k) RAE 6.1 (SEQ ID NO:24);
- l) RAE 7.D (SEQ ID NO:25);
- m) RAE 7.D-1 (SEQ ID NO:26);
- n) RAE 40.1-6 (SEQ ID NO:27);
- o) RAE 40.1-5 (SEQ ID NO:28);
- p) RAE 40.1-4 (SEQ ID NO:29);
- q) RAE 40.D (SEQ ID NO:30);
- r) RAE 40.1 (SEQ ID NO:31);
- s) RAE 61.1 (SEQ ID NO:32);
- t) RAE 80.1 (SEQ ID NO:33);
- u) RAE 45.1 (SEQ ID NO:34);

- 5 v) RAE 75.1 (SEQ ID NO:35);  
w) RAE 62.1 (SEQ ID NO:36);  
x) RAE 69.1 (SEQ ID NO:37);  
y) RAE 69.1-1 (SEQ ID NO:38);  
z) RAE 69.1-2 (SEQ ID NO:39);  
a') RAE 69.1-3 (SEQ ID NO:40);  
b') RAE 70.1-3 (SEQ ID NO:41);  
c') RAE 70.1-2 (SEQ ID NO:42);  
d') RAE 71.1 (SEQ ID NO:45);  
10 e') RAE 65.1 (SEQ ID NO:46);  
f') RAE 63.1 (SEQ ID NO:47);  
g') RAE 76.1 (SEQ ID NO:48);  
h') RAE 27.1 (SEQ ID NO:49);  
i') RAE 66.1 (SEQ ID NO:50);  
15 j') RAE 66.1-1 (SEQ ID NO:51);  
k') RAE 66.1-2 (SEQ ID NO:52);  
l') RAE 66.1-3 (SEQ ID NO:53);  
m') RAE 64.1-3 (SEQ ID NO:54);  
n') RAE 64.1-2 (SEQ ID NO:55);  
20 o') RAE 64.1-1 (SEQ ID NO:56);  
p') RAE 64.1 (SEQ ID NO:57);  
q') RAE 73.1 (SEQ ID NO:58);  
r') RAE 74.1 (SEQ ID NO:59);  
s') RAE 74.1-1 (SEQ ID NO:60);  
25 t') RAE 29.1 (SEQ ID NO:61);  
u') RAE 29.1-1 (SEQ ID NO:62);  
v') RAE 28+29 (SEQ ID NO:63);  
w') RAE 29.1-2 (SEQ ID NO:64);  
x') RAE 29.1-3 (SEQ ID NO:65);  
30 y') RAE 29.1-4 (SEQ ID NO:66);  
z') RAE 28.1-3 (SEQ ID NO:67);  
a'') RAE 28.1-2 (SEQ ID NO:68);  
b'') RAE 28.1-1 (SEQ ID NO:69);  
c'') RAE 28.1 (SEQ ID NO:70);  
35 d'') RAE 20.1 (SEQ ID NO:71);  
e'') RAE 20.1-3 (SEQ ID NO:72);  
f'') RAE 20.1-2 (SEQ ID NO:73);  
g'') RAE 20.1-1 (SEQ ID NO:74);  
h'') RAE 21.1 (SEQ ID NO:75);

- i") RAE 17.1 (SEQ ID NO:76);  
j") RAE 55.1 (SEQ ID NO:77);  
k") RAE 76.6 (SEQ ID NO:78);  
l") RAE 67.15 (SEQ ID NO:79);  
5 m") RAE 45.15 (SEQ ID NO:80); and  
n") RAE 27.15 (SEQ ID NO:81).

20. An isolated peptide comprising at least two regions, each region comprising at least one T cell epitope of a protein allergen of *Ambrosia artemisiifolia*, said regions derived  
10 from the same or from different protein allergens of *Ambrosia artemisiifolia*, said regions each comprising all or a portion of an amino acid sequence selected from the group consisting of:

- 15 a) AMB 1-1.1 (SEQ ID NO:85);  
b) AMB 1-2.1 (SEQ ID NO:86);  
c) AMB 1-3.1 (SEQ ID NO:87);  
d) AMB 1-4.1 (SEQ ID NO:84);  
e) AMB 1-5.1 (SEQ ID NO:83);  
f) AMB 1-6.1 (SEQ ID NO:82);  
20 g) AMB 2-4.1 (SEQ ID NO:90);  
h) AMB 2-3.1 (SEQ ID NO:91);  
i) AMB 2-5.1 (SEQ ID NO:92);  
j) AMB 2-6.1 (SEQ ID NO:93);  
k) AMB 2-2.1 (SEQ ID NO:94);  
25 l) AMB 2-1.1 (SEQ ID NO:95);  
m) RAE 70.1-1 (SEQ ID NO:43);  
n) AMB 2-7.1 (SEQ ID NO:96);  
o) AMB 2-8.1 (SEQ ID NO:97);  
p) AMB 2-9.1 (SEQ ID NO:98);  
30 q) AMB 2-10.1 (SEQ ID NO:99);  
r) AMB 2-11.1 (SEQ ID NO:100);  
s) RAE 70.1 (SEQ ID NO:44);  
t) AMB 3-4.1 (SEQ ID NO:103);  
u) AMB 3-5.1 (SEQ ID NO:102);  
35 v) AMB 3-3.1 (SEQ ID NO:104);  
w) AMB 3-2.1 (SEQ ID NO:105);  
x) AMB 3-1.1 (SEQ ID NO:106);  
y) AMB 4-8.1 (SEQ ID NO:109);  
z) AMB 4-9.1 (SEQ ID NO:110);